Doc Code: AP.PRE.REQ

PTO/SB/33 (07-05)
Approved for use through xx/xx/200x. OMB 0651-00xx
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 16051-5US CC/DBB/jrl

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

on _____

Signature _____

Typed or printed name _____

Application Number	Filed
10/661,099	September 12, 2003

First Named Inventor: VAILLANT, Andrew

Art Unit	Examiner
1648	Louise Z. Wang

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☒ attorney or agent of record. Registration number 47,352
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

Signature

Christian Cawthorn
Typed or printed name

(514) 847-4256
Telephone number

February 23, 2007
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☒ *Total of 1 forms are submitted.

File No. 16051-5US CC/DBB/jrl

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Andrew VAILLANT et al.
Serial Number:	10/661,099
Filing Date:	September 12, 2003
For:	ANTIVIRAL OLIGONUCLEOTIDES TARGETING HIV
Art Unit:	1648
Examiner:	Louise Z. WANG
Agent:	Cawthorn, Christian (514) 847-4256

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Assistant Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
U. S. A.

Sir:

Please find enclosed herewith form PTO/SB/33 for the pre-appeal brief request for review. Please consider the reasons below for which the review is being requested.

A Notice of Appeal is being filed concurrently.

REASONS:

Claims 1, 2, 14-20 and 26-32 have been rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification. Further, Claims 1, 2, 14-20, and 26-32 have been rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement.

Regarding the first rejection of claims 1, 2, 14-20 and 26-32 under 35 U.S.C. § 112, first paragraph, the Examiner has maintained her rejection of the claims as containing subject matter which was not described in the specification. The Examiner further stated that the response submitted on December 5, 2006 is insufficient to overcome this rejection. The declaration presented an SIV model in non-human primates and a FLV disease mice model, which, according to the Examiner, is nonanalogous to the claimed method of prophylaxis and treatment of HIV in humans. Contrary to the Examiner's position, Applicants respectfully point out that, as submitted

Assistant Commissioner for Patents

previously in the Declaration of Dr. Jean-Marc Juteau (June 8, 2006), the *in vivo* SIV model is the only model available unless Applicants initiate Clinical phase III trials. For the time being, the SIV model shows 98% identity with HIV-2, which is thus by far the best model to prove efficacy and utility of the present invention. It is believed that in order to convince the Examiner of the enablement of the present invention, clinical trials must be initiated. Requesting clinical trial results to demonstrate enablement of the present invention is unreasonable and represents an undue burden, burden that does not exist in any other field of invention. Applicants respectfully submit that it is stated in the Manual of Patent Examining Procedure (MPEP 2107.03, section IV) that:

> "Office personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials. There is no decisional law that requires an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders."

Applicants wish to submit that, only when the pre-clinical data is promising, a company takes a decision on whether to begin the long and costly process of clinical trials. Most companies file for and receive patents for the commercial use of the compound that they are developing during pre-clinical trials in order to not only protect their invention, but also to reassure investors that the invention which will be undergoing clinical phase trials is patented. Assuming the company decides to pursue human studies, it must first submit an Investigational New Drug (IND) application to the FDA for approval. The IND must provide pre-clinical data of sufficient quality to justify the testing of the drug in humans. It is believed that in order for the present invention to be commercially and financially liable, Applicants needs to file a patent application before submitting an IND application to the FDA. Applicants believe that the Examiner is not examining the present application in terms of its patentability, but in terms of its liability to pursue human studies, which is believed to be the role of the FDA and not of the USPTO. Consequently, Applicants feel that, in view of the arguments presented by the Examiner, it is easier to obtain an FDA approval to start clinical phase trials then meeting the criteria of patentability imposed by the Examiner.

Applicants also submitted in the response dated December 5, 2006, several scientific publications demonstrating the predictability of the model consisting of a macaque infected with

Assistant Commissioner for Patents

SIV and SIV-derived (chimeric) viruses, wherein the activity of antiviral drugs that are known to be active in humans, FDA approved and commercially available was demonstrated (i.e. PMEA, PMPA, efavirenz, AZT, 3TC and lopinavir/ritonavir; references of Silvera *et al.*, 2000; Van Rompay *et al.*, 2001; Hofman *et al.*, 2004; Yoshimura *et al.*, 2003; and North *et al.*, 2005). The Examiner acknowledged that these references submitted present results on investigation drugs solely for the treatment of HIV infection, but she argued that they do not teach the predictive value of primate models for HIV vaccine. Further, Applicants wish to also add that the NIH/NIAID offers the service of testing drugs in the SIV models for the development of AIDS therapy. This means that a US government agency like the NIH/NIAID currently recognizes that the SIV macaque model is useful for testing the efficacy of novel drugs and is an acceptable model. The Examiner further cited the reference of Jefferys, 2005 (Merck vaccine candidate) in order to support her argument. In this respect, Applicants wish to point out that the present application is NOT claiming a VACCINE. This argument presented by the Examiner is believed to be irrelevant to the present invention. A person skilled in the art would acknowledge that a vaccine comprises an antigen or antigens (or a DNA coding for an antigen) stimulating the immune system which will target such antigen(s) displayed on a microorganism, (or on a cell, or as a molecule e.g. a toxine) in order to destroy the microorganism or inhibit its growth cycle. The present application teaches antiviral compounds that do not act as an antigen stimulating the immune system. In the case of antiviral compounds or drugs, replication cycle of the virus is targeted by the compound itself and not through stimulation of the immune system. Consequently, the present application is NOT teaching or claiming a VACCINE, the present application is claiming a method for the prophylaxis or treatment of a HIV infection in a subject, comprising administering a therapeutically effective amount of at least one pharmacologically acceptable oligonucleotide at least 30 nucleotides in length, wherein said oligonucleotide has an anti-HIV activity and wherein the anti-HIV activity of said oligonucleotide occurs principally by a sequence independent mode of action.

It is thus believed that the Applicants provided data, both from *in vitro* assays and animal tests, to support the asserted utility, and an explanation on how that data supports the asserted utility. In view of the above, Applicants respectfully submit that the 35 U.S.C. § 112, first paragraph, rejection is improper and requests that it be withdrawn.

Assistant Commissioner for Patents

Regarding rejection of claims 1, 2, 14-20, and 26-32 under 35 USC § 112, first paragraph, as failing to comply with the written description requirement, the Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner is of the opinion that the specification does not sufficiently describe the genus of oligonucleotides that are at least 30 nucleotides in length, which encompasses 1.1 x 10E18 variants. The Examiner mentioned that the specification does not provide substantial evidence and factual findings for an unpredictable art such as HIV vaccine in humans. The Applicants respectfully disagree and submit that, as defined on page 14 of the present description, the term "randomer" is intended to mean a single stranded DNA having a wobble (N) at every position, such as NNNNNNNNNN. Each base is synthesized as a wobble, such that the randomer oligonucleotides of the present invention actually consist of a population of different randomly-generated sequences of the same size. By the nature of the preparation used to produce them, a sequence complementary mode of action cannot occur. It is believed that a person skilled in the art would recognize that the only common feature between the 26 oligonucleotides having a specific sequence and the 19 randomer oligonucleotides disclosed in Table 1 is that they have anti-HIV activity occurring by a sequence independent mode of action. As disclosed on page 11 of the present description, in a 15 μmol preparation of a randomer oligonucleotide containing 32 nucleotides in length, this preparation will have at most 2 copies of every possible sequence of nucleotides. Thus, the presence of 2 copies of a specific sequence cannot account for the response observed in the present application. For the disclosed 19 randomer oligonucleotides of Table 1, by the nature of the preparation used to produce them, a sequence complementary mode of action cannot occur. Applicants wish to point out that even the Examiner acknowledged in the Advisory Action issued on January 23, 2007, that the list of 26 nucleotides and 19 randomers disclosed in the present description does represent the entire genus. In addition, Applicants respectfully point out that it is stated in the Manual of Patent Examining Procedure that:

> "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are

Assistant Commissioner for Patents

representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the genus" (Manual of Patent Examining Procedure 2163.05)."

It is therefore believed that the present description discloses 45 oligonucleotide sequences, of which 26 have nucleotide sequence identity and 19 are randomer oligonucleotide sequences. In addition, the present description discloses 45 oligonucleotide sequences of differing lengths. The 19 randomer oligonucleotides, acting by a sequence independent mode of action, are by themselves a representative number of species, and of the genus itself, as they are independent of any specific sequence. Thus, it is believed that the present application teaches a sufficient and/or representative number of varieties of species to reflect the complete genus. Finally, regarding the Examiner's argument that the specification does not provide substantial evidence and factual findings for an unpredictable art such as HIV vaccine in humans, Applicants reiterate the fact presented hereinabove that the present application is NOT teaching or claiming a VACCINE.

In view of the foregoing, Applicants respectfully submit that the 35 U.S.C. § 112, first paragraph, rejection is improper and requests that it be withdrawn.

It is submitted, therefore, that the claims are in condition for allowance, and prompt and favorable action in the form of a Notice of Allowance is earnestly solicited.

Respectfully submitted,

Date: February 23, 2007

By: _____

Christian Cawthorn, Reg. No. 47,352
Agent for Applicants
Tel: (514) 847-4256

OGILVY RENAULT LLP
1981 McGill College, Suite 1600
Montreal, Quebec H3A 2Y3
CANADA